# Intravenous Iron Therapy

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## Introduction

Iron plays an essential role in human physiology and is necessary for red blood cell production. It is the most common nutritional deficiency worldwide, both in developed and developing countries.

The challenge of treating iron deficiency is related to the toxicity of iron in its elemental state, the required dose, and the desired rate of repletion. Intravenous (IV) iron is increasingly being used for the treatment of iron deficiency anaemia (IDA) when oral iron is ineffective or poorly tolerated, and when it or blood transfusion is inappropriate.

## Indications for the use of IV iron

**Intolerability to, or Ineffectiveness of Oral Iron**

IV iron can overcome the blocking of iron absorption from the gastrointestinal tract (GIT) and immobilization of stored iron which occurs in chronic disease / inflammation.

**Excessive Ongoing Blood Loss**

Parental iron can be used in iron-deficient patients when the level of bleeding exceeds the ability of the GIT to absorb iron. (The maximum absorptive capacity of iron by the GIT from oral iron preparations is 25 mg/day)

**Inflammatory Bowel Disease (IBD)**

IV iron can be considered in patients with IBD in the following situations:

(i) anaemia and unresponsiveness to, or tolerance of, oral iron
(ii) need for quick recovery from anaemia
(iii) adjuvant to the use of erythropoietin

**Chronic Kidney Disease (CKD)**

IV iron is currently standard practice in both dialysis and non-dialysis associated CKD patients.

**Cancer Patients**

Prospective studies support the observation that IV iron synergizes with erythropoiesis-stimulating agents (ESAs) in anaemic cancer patients both on and off chemotherapy.

**Heart Failure (controversial)**

While evidence suggests that IV iron provides symptomatic benefit in selected patients with heart failure, the long term effects of such treatment are not known.

**Pregnancy (controversial)**

IV iron is contra-indicated in the 1st trimester as no trials has confirmed its safety; and no parenteral iron has been given US FDA category “A” rating for use in pregnancy. However, there is some published evidence on the safety of IV iron in pregnancy.
Available IV Iron Preparations

The table below lists most of the parenteral iron formulations approved for use throughout the world¹.

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Iron Dextran (HMW)</th>
<th>Iron Dextran (LMW)</th>
<th>Ferric Gluconate</th>
<th>Iron Sucrose</th>
<th>Ferumoxytol</th>
<th>Ferric Carboxymaltose</th>
<th>Iron Isomaltoside</th>
</tr>
</thead>
<tbody>
<tr>
<td>DexFerrum</td>
<td>100 mg</td>
<td>100 mg</td>
<td>125 mg</td>
<td>200 mg</td>
<td>510 mg</td>
<td>1 000 mg if patient weight &gt; 66kg</td>
<td>No</td>
</tr>
<tr>
<td>Cosmofer/INFeD</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Ferrlecit</td>
<td>Yes (Only approved in Europe)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Venofer</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Feraheme</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Ferinject/Injectafer</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Monofer (Europe only)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>TDI Possible</td>
<td>Yes</td>
<td>Yes (Only approved in Europe)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pre-medication</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Test Dose Required</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Iron Concentration (mg/mL)</td>
<td>50</td>
<td>50</td>
<td>12.5</td>
<td>20</td>
<td>30</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Vial Volume (mL)</td>
<td>1 and 2</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>17</td>
<td>2 and 10</td>
<td>1, 5 and 10</td>
</tr>
</tbody>
</table>

HMW = high molecular weight; LMW = low molecular weight; TDI = total dose infusion
* HMW Iron dextran preparations are NOT recommended due to higher incidence of adverse reactions.
# LMW Iron dextran (Cosmofer) and Iron Sucrose (Venofer) are both available in South Africa.
o Ferumoxytol is approved by the US FDA for iron replacement in patients with IDA and CKD.
? Ferric carboxymaltose and Iron Isomaltoside are currently only available in certain European countries.

Adverse Events

Each of the available IV iron formulations has been associated with anecdotal reports of life-threatening adverse events. HMW Iron dextran is associated with a considerably higher incidence of adverse events than LMW preparations and should be used with caution.

Iron infusions should be given only at appropriately staffed sites with resuscitation facilities.

A. Hypersensitivity Reactions (HSRs)
Systemic effects of IV iron include self-limiting fever, arthralgias and myalgias, usually within 24 hours of infusion. These resolve without therapy.

Acute hypersensitivity reactions during iron infusion are rare but potentially life-threatening. HSRs can be classified as mild, moderate or severe/life-threatening.

Factors increasing the risk and/or severity of HSRs to IV iron infusions include:
- Previous reaction to IV iron
- Fast infusion rate
- History of other drug allergy or allergies*
- Severe asthma or eczema*
- Mastocytosis
- Severe respiratory or cardiac disease
- Old age
- Treatment with beta-blockers, ACE-inhibitors
- Pregnancy (1st trimester) *
- Systemic inflammatory disease (e.g. rheumatoid arthritis, systemic lupus erythematosus)
- Anxiety (patient or staff)

* Pre-medicate with 125 mg IV methylprednisolone
# IV iron is contra-indicated early in pregnancy

The algorithm below outlines the grading and management of hypersensitivity reactions.

**B. Risk Of Infection**

IV iron should NOT be used in patients with active infection. However, current literature does not support the contention that the use of IV iron is associated with an increased risk of infection.
Conclusions

- There are a number of indications for the use of parenteral iron rather than oral iron preparations, particularly in the presence of anaemia of chronic disease, where it appears to overcome the block of iron absorption from the gastrointestinal tract and immobilization of stored iron.
- There has been major progress in the development of IV iron preparations with the potential advantage of total dose infusion and complete repletion in a single sitting.
- The historical reluctance to use IV iron can be partly traced to concerns about serious adverse events associated with earlier IV iron preparations, such as HMW Iron dextran. However, with the use of risk minimization measures and avoidance of HMW Iron dextran, serious adverse events with IV iron are extremely rare.

References